JCB

THE JOURNAL OF CELL BIOLOGY

EDITOR-IN-CHIEF
TOM MISTELI

EDITORS
PIER PAOLO DI FIORE
ELAINE FUCHS
ALAN HALL
REBECCA HEALD
IRA MELLMAN
JODI NUNNARI
LOUIS F. REICHARDT
KENNETH M. YAMADA
JUNYING YUAN

NEWS EDITOR
BENJAMIN SHORT

REVIEWS EDITOR
PRIYA PRAKASH BUDDE

EDITORIAL BOARD

JOHN AITCHISON
NORMA ANDREWS
BEN BARRES
HUGO BELLEN
VANN BENNETT
JEFFREY BENOVIC
MONICA BETTENCOURT-DIAS
CÉDRIC BLANPAIN
TONY BRETSCHER
MARIANNE BRONNER
DON W. CLEVELAND
PASCALE COSSART
GAUDENZ DANUSER
PIETRO DE CAMILLI
TITIA DE LANGE
ARSHAD DESAI
RAY DESHAIES
IVAN DIKIC
STEVE DOXSEY
WILLIAM EARNSHAW
SCOTT EMR
JEFFREY ESKO
HIRONORI FUNABIKI
LARRY GERACE
FRANK GERTLER
DAVID GILBERT
MARK GINSBERG
GILLIAN GRIFFITHS
SERGIO GRINSTEIN
ULRICH HARTL
RAMANUJAN HEGDE
NOBUTAKA HIROKAWA
ERIKA HOLZBAUR
ARTHUR HORWICH
ALAN RICK HORWITZ
M. ANDREW HOYT
MARTIN HUMPHRIES
ANNA HUTTENLOCHER
LUISA IRUELA-ARISPE
GERARD KARSENTY
ALEXEY KHODJAKOV
AKIHIRO KUSUMI
THOMAS LANGER
JEANNE LAWRENCE
VERONIQUE LEFEBVRE
DANNY LEW
HAIFAN LIN
JIRI LUKAS
IAN MACARA
VIVEK MALHOTRA
JOAN MASSAGUE
JACOPO MELDOLESI
RANDALL T. MOON
SEAN MUNRO
ANDRÉ NUSSENZWEIG
KAREN OEGEMA
ERIC OLSON
LESLIE PARISE
ROY PARKER
ROBERT G. PARTON
MARK PEIFER
THOMAS RANDO
DANIEL B. RIFKIN
DAVID RON
MICHAEL ROUT
MICHAEL RUDNICKI
ERIK SAHAI
JOSHUA SANES
JOSEPH SCHLESSINGER
DANNY SCHNELL
TRINA SCHROER
MARTIN SCHWARTZ
JEAN SCHWARZBAUER
JOAN STEITZ
HARALD STENMARK
ANDREAS STRASSER
RON VALE
WIM VERMEULEN
LOIS WEISMAN
MATT WELCH
TIM YEN
TAMOTSU YOSHIMORI
RICHARD YOULE
MARINO ZERIAL
YIXIAN ZHENG

EXECUTIVE EDITOR
LIZ WILLIAMS
Phone: 212-327-8011
Fax: 212-327-8576
email: lwilliams@rockefeller.edu

ASSOCIATE EDITOR
PAMELA CARPENTIER
Phone: 212-327-8571
Fax: 212-327-8576
email: pamela.carpentier@rockefeller.edu

EDITORIAL ASSISTANTS
JANINE FLERI
LINDSEY HOLLANDER
DIEDRA HOWSON-BARKER
SATI MOTIERAM
Phone: 212-327-8581
Fax: 212-327-8576
email: jcellbiol@rockefeller.edu

COPYEDITING AND PRODUCTION
email: jcb@rockefeller.edu

PREFLIGHT COORDINATOR
LAURA SMITH

COPY EDITORS
MARGUERITE SPELLMAN
MARY VASQUEZ

ASSISTANT PRODUCTION EDITOR
JASON ROTHAUSER

PRODUCTION EDITOR
GREGORY E. KOUTROUBY

NEWS PRODUCTION EDITOR
RITA E. SULLIVAN

COPY EDITING COORDINATOR
CAMILLE CLOWERY

PRODUCTION COORDINATOR
ERINN A. GRADY

PRODUCTION DIRECTOR
ROBERT J. O'DONNELL

THE ROCKEFELLER UNIVERSITY PRESS
QUALITY AND INTEGRITY

VOLUME 199, 2012

JCB
THE JOURNAL OF CELL BIOLOGY
VOL. 199, NO. 1, OCTOBER 1, 2012

NEWS

In This Issue

2
- B23 steals to stop cell-killing pair
- microRNA's big role in preventing tumors
- Dynein's helper not so helpful

M. Leslie

In Focus

3
- Cytoskeleton key

M. Leslie

People & Ideas

4
- Cédric Blanpain: The stories stem cells tell

C. Sedwick

Editorials

7 Cell biology: At the center of modern biomedicine
Priya Prakash Budde, Elizabeth H. Williams, and Tom Misteli

Features

9 Progeria: Translational insights from cell biology
Leslie B. Gordon, Kan Cao, and Francis S. Collins

15 The genesis of Zelboraf: Targeting mutant B-Raf in melanoma
Matthew J. Davis and Joseph Schlessinger

21 Antisense-based therapy for the treatment of spinal muscular atrophy
Frank Rigo, Yimin Hua, Adrian R. Krainer, and C. Frank Bennett

RESEARCH ARTICLES

Reports

27 Mad2 and the APC/C compete for the same site on Cdc20 to ensure proper chromosome segregation
Daisuke Izawa and Jonathon Pines

39 Structural basis of the junctional anchorage of the cerebral cavernous malformations complex
Alexandre R. Gingras, Jian J. Liu, and Mark H. Ginsberg

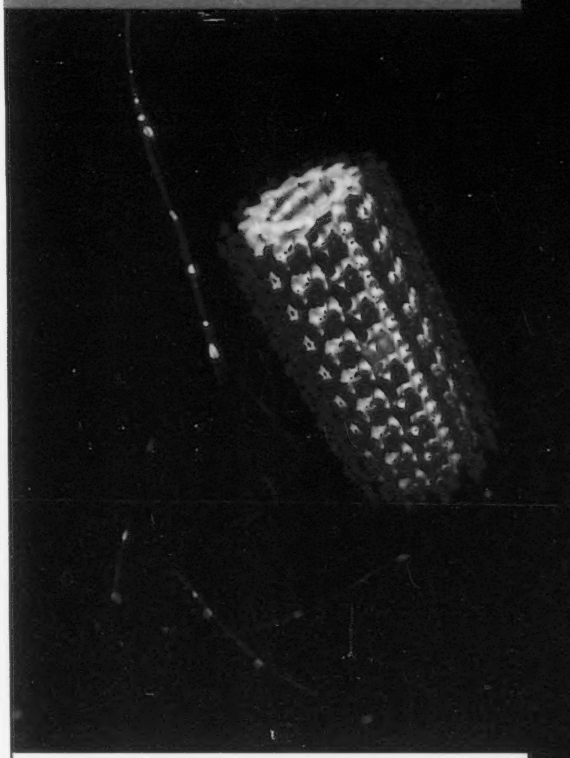
Articles

49 PML promotes MHC class II gene expression by stabilizing the class II transactivator
Tobias Ulbricht, Mohammad Alzrigat, Almut Horch, Nina Reuter, Anna von Mikecz, Viktor Steimle, Eberhard Schmitt, Oliver H. Krämer, Thomas Stamminger, and Peter Hemmerich

65 S-nitrosylation of B23/nucleophosmin by GAPDH protects cells from the SIAH1–GAPDH death cascade
Sang Bae Lee, Chung Kwon Kim, Kyung-Hoon Lee, and Jee-Yin Ahn

77 Differentiation-associated microRNAs antagonize the Rb–E2F pathway to restrict proliferation
Matteo J. Marzi, Eleonora M. R. Puggioni, Valentina Dall'Olio, Gabriele Bucci, Loris Bernard, Fabrizio Bianchi, Marco Crescenzi, Pier Paolo Di Fiore, and Francesco Nicassio

Articles with related stories in the IN THIS ISSUE section have page numbers in RED; articles related to the IN FOCUS feature have page numbers in BLUE.



On the cover

Shen et al. investigate how the actin-nucleating protein WHAMM coordinates the actin and microtubule cytoskeletons during membrane remodeling. In the foreground, a 3D reconstruction shows the structure of WHAMM molecules (green) bound to a microtubule (gray). A single WHAMM molecule is colored pink. The background fluorescence image shows that WHAMM-decorated microtubules (green) can recruit lipid vesicles (red).
Image courtesy of Qing-Tao Shen.
See page 111.

97 Cortical dynein is critical for proper spindle positioning in human cells
Sachin Kotak, Coralie Busso, and Pierre Gönczy

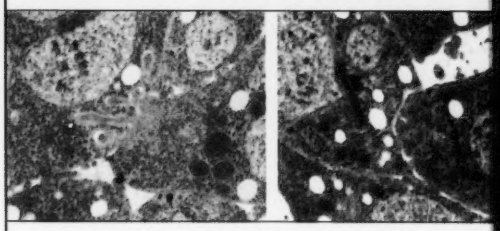
111 Structural insights into WHAMM-mediated cytoskeletal coordination during membrane remodeling
Qing-Tao Shen, Peter P. Hsiue, Charles V. Sindelar, Matthew D. Welch, Kenneth G. Campellone, and Hong-Wei Wang

125 Biogenesis of the mitochondrial Hsp70 chaperone
Marta Blamowska, Walter Neupert, and Kai Hell

137 The Cbp3–Cbp6 complex coordinates cytochrome *b* synthesis with bc_1 complex assembly in yeast mitochondria
Steffi Gruschke, Katharina Römpler, Markus Hildenbeutel, Kirsten Kehrein, Inge Kühl, Nathalie Bonnefoy, and Martin Ott

151 The role of retrograde intraflagellar transport in flagellar assembly, maintenance, and function
Benjamin D. Engel, Hiroaki Ishikawa, Kimberly A. Wemmer, Stefan Geimer, Ken-ichi Wakabayashi, Masafumi Hirono, Branch Craige, Gregory J. Pazour, George B. Witman, Ritsu Kamiya, and Wallace F. Marshall

169 Group I PAKs function downstream of Rac to promote podosome invasion during myoblast fusion in vivo
Rui Duan, Peng Jin, Fengbao Luo, Guofeng Zhang, Nathan Anderson, and Elizabeth H. Chen



In a wild-type *Drosophila* embryo (left), a fusion-competent myoblast (pseudocolored pink) inserts actin-rich fingers into a neighboring multinucleate myotube to initiate fusion of the two cells. These invasive fingers are absent, and fusion is defective, in embryos lacking the p21-activated kinase DPak3 (right). **See page 169.**

JCB
THE JOURNAL OF CELL BIOLOGY
VOL. 199, NO. 2, OCTOBER 15, 2012

NEWS

In This Issue

188
- The mystery of the (not) missing coenzyme
- Sec and Tat share the workload
- Tiam1 increases turnover
  B. Short

In Focus

189
- Fyn regeneration
  B. Short

People & Ideas

190
- Laurie Boyer: Stem cell circuitry for commitment
  C. Sedwick

Features

193 Hedgehog pathway inhibition and the race against tumor evolution
Scott X. Atwood, Anne Lynn S. Chang, and Anthony E. Oro

199 Fixing cystic fibrosis by correcting CFTR domain assembly
Tsukasa Okiyoneda and Gergely L. Lukacs

205 Exploring the therapeutic space around NAD^+
Riekelt H. Houtkooper and Johan Auwerx

REVIEWS

Comments

211 Guilt by association: What p120-catenin has to hide
Mirna Perez-Moreno and Elaine Fuchs

RESEARCH ARTICLES

Reports

215 The submitochondrial distribution of ubiquinone affects respiration in long-lived *Mclk1*$^{+/-}$ mice
Jérôme Lapointe, Ying Wang, Eve Bigras, and Siegfried Hekimi

225 Early redox, Src family kinase, and calcium signaling integrate wound responses and tissue regeneration in zebrafish
Sa Kan Yoo, Christina M. Freisinger, Danny C. LeBert, and Anna Huttenlocher

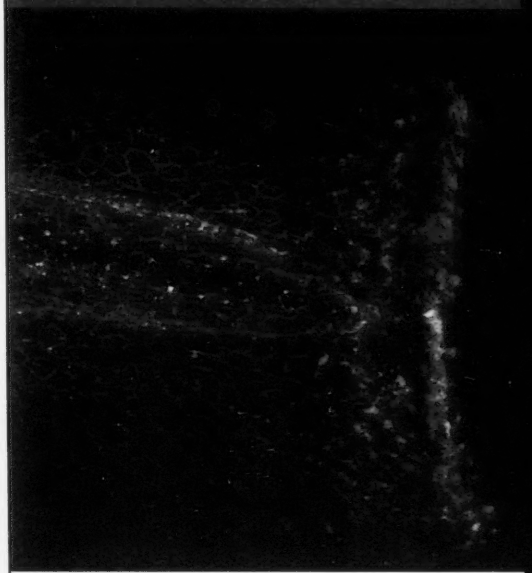
Articles

235 PARP1 promotes nucleotide excision repair through DDB2 stabilization and recruitment of ALC1
Alex Pines, Mischa G. Vrouwe, Jurgen A. Marteijn, Dimitris Typas, Martijn S. Luijsterburg, Medine Cansoy, Paul Hensbergen, André Deelder, Anton de Groot, Syota Matsumoto, Kaoru Sugasawa, Nicolas Thoma, Wim Vermeulen, Harry Vrieling, and Leon Mullenders

251 Haspin inhibitors reveal centromeric functions of Aurora B in chromosome segregation
Fangwei Wang, Natalia P. Ulyanova, John R. Daum, Debasis Patnaik, Anna V. Kateneva, Gary J. Gorbsky, and Jonathan M.G. Higgins

269 A small-molecule inhibitor of Haspin alters the kinetochore functions of Aurora B
Anna De Antoni, Stefano Maffini, Stefan Knapp, Andrea Musacchio, and Stefano Santaguida

Articles with related stories in the IN THIS ISSUE section have page numbers in RED; articles related to the IN FOCUS feature have page numbers in BLUE; articles with COMMENTS have page numbers in GREEN.



On the cover

30 min after injury, activated Src family kinases (green) and ERK (magenta) are apparent in the epithelium of a wounded zebrafish tail fin. Yoo et al. demonstrate that these early signaling events, as well as a short burst of intracellular calcium release, are required for the regeneration of the fin several days later.
Image © 2012 Yoo et al.
See page 225.

285 Cdk1 and Plk1 mediate a CLASP2 phospho-switch that stabilizes kinetochore–microtubule attachments
Ana R.R. Maia, Zaira Garcia, Lilian Kabeche, Marin Barisic, Stefano Maffini, Sandra Macedo-Ribeiro, Iain M. Cheeseman, Duane A. Compton, Irina Kaverina, and Helder Maiato

303 Co-operation between different targeting pathways during integration of a membrane protein
Rebecca Keller, Jeanine de Keyzer, Arnold J.M. Driessen, and Tracy Palmer

317 Rap1-interacting adapter molecule (RIAM) associates with the plasma membrane via a proximity detector
Joseph P. Wynne, Jinhua Wu, Wenjuan Su, Adam Mor, Nikolaos Patsoukis, Vassiliki A. Boussiotis, Stevan R. Hubbard, and Mark R. Philips

331 Tiam1 interaction with the PAR complex promotes talin-mediated Rac1 activation during polarized cell migration
Shujie Wang, Takashi Watanabe, Kenji Matsuzawa, Akira Katsumi, Mai Kakeno, Toshinori Matsui, Feng Ye, Kazuhide Sato, Kiyoko Murase, Ikuko Sugiyama, Kazushi Kimura, Akira Mizoguchi, Mark H. Ginsberg, John G. Collard, and Kozo Kaibuchi

347 miR-24 triggers epidermal differentiation by controlling actin adhesion and cell migration
Ivano Amelio, Anna Maria Lena, Giuditta Viticchiè, Ruby Shalom-Feuerstein, Alessandro Terrinoni, David Dinsdale, Giandomenico Russo, Claudia Fortunato, Elena Bonanno, Luigi Giusto Spagnoli, Daniel Aberdam, Richard Austen Knight, Eleonora Candi, and Gerry Melino

365 p120-catenin binding masks an endocytic signal conserved in classical cadherins
Benjamin A. Nanes, Christine Chiasson-MacKenzie, Anthony M. Lowery, Noboru Ishiyama, Victor Faundez, Mitsuhiko Ikura, Peter A. Vincent, and Andrew P. Kowalczyk

381 Localization of Usher 1 proteins to the photoreceptor calyceal processes, which are absent from mice
Iman Sahly, Eric Dufour, Cataldo Schietroma, Vincent Michel, Amel Bahloul, Isabelle Perfettini, Elise Pepermans, Amrit Estivalet, Diane Carette, Asadollah Aghaie, Inga Ebermann, Andrea Lelli, Maria Iribarne, Jean-Pierre Hardelin, Dominique Weil, José-Alain Sahel, Aziz El-Amraoui, and Christine Petit

Sahly et al. reveal that proteins associated with the hearing and vision loss of Usher syndrome, including protocadherin-15 (green), localize to microvillus-like calyceal processes at the base of the outer segments of rod and cone photoreceptors in primates (cone outer segments are labeled red). Mouse photoreceptors lack calyceal processes, potentially explaining why mice lacking Usher syndrome proteins don't display retinal degeneration.
Image © 2012 Sahly et al.
See page 381.

JCB
THE JOURNAL OF CELL BIOLOGY
VOL. 199, NO. 3, OCTOBER 29, 2012

NEWS

In This Issue

402 • HIV's kinesin chauffeur
• Only skin deep, thanks to microtubules
• N-WASP helps cancer cells open up
M. Leslie

In Focus

403 • Stay-at-home transcription factor saves axons
M. Leslie

People & Ideas

404 • Fumiyo Ikeda: Ubiquitin lines up for action
C. Sedwick

Features

407 Discovering the first microRNA-targeted drug
Morten Lindow and Sakari Kauppinen

413 The discovery of natalizumab, a potent therapeutic for multiple sclerosis
Lawrence Steinman

417 Hypertrophic cardiomyopathy: Translating cellular cross talk into therapeutics
Polakit Teekakirikul, Robert F. Padera, J.G. Seidman, and Christine E. Seidman

REVIEWS

Comments

423 Using force to visualize conformational activation of integrins
David Boettiger

RESEARCH ARTICLES

Reports

425 Phosphocaveolin-1 is a mechanotransducer that induces caveola biogenesis via Egr1 transcriptional regulation
Bharat Joshi, Michele Bastiani, Scott S. Strugnell, Cecile Boscher, Robert G. Parton, and Ivan R. Nabi

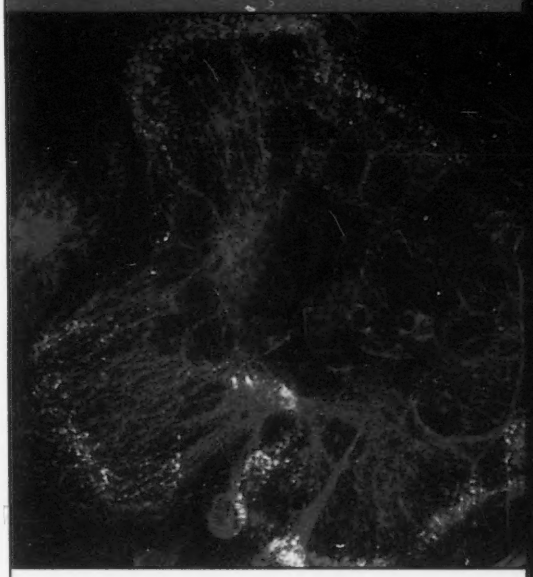
Articles

437 Local axonal function of STAT3 rescues axon degeneration in the *pmn* model of motoneuron disease
Bhuvaneish Thangaraj Selvaraj, Nicolas Frank, Florian L.P. Bender, Esther Asan, and Michael Sendtner

453 Rbms3 functions in craniofacial development by posttranscriptionally modulating TGF-β signaling
Chathurani S. Jayasena and Marianne E. Bronner

467 Critical role for the kinesin KIF3A in the HIV life cycle in primary human macrophages
Raphaël Gaudin, Bruna Cunha de Alencar, Mabel Jouve, Stefano Bèrre, Emmanuel Le Bouder, Michael Schindler, Aditi Varthaman, François-Xavier Gobert, and Philippe Benaroch

Articles with related stories in the IN THIS ISSUE section have page numbers in RED; articles related to the IN FOCUS feature have page numbers in BLUE; articles with COMMENTS have page numbers in GREEN.



On the cover

Macrophages infected with HIV-1 (green) develop into giant cells with multiple nuclei (blue) and highly organized networks of microtubules (red) and actin (cyan). Gaudin et al. reveal that the microtubule-based kinesin motor KIF3A is important for the intracellular transport of virus-containing compartments and for the release of HIV-1 from infected macrophages.

Image © 2012 Gaudin et al.

See page 467.

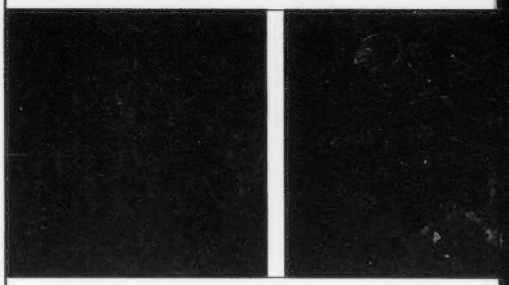
481 TspanC8 tetraspanins regulate ADAM10/Kuzbanian trafficking and promote Notch activation in flies and mammals
Emmanuel Dornier, Franck Coumailleau, Jean-François Ottavi, Julien Moretti, Claude Boucheix, Philippe Mauduit, François Schweisguth, and Eric Rubinstein

497 Observing force-regulated conformational changes and ligand dissociation from a single integrin on cells
Wei Chen, Jizhong Lou, Evan A. Evans, and Cheng Zhu

513 Noncentrosomal microtubules and type II myosins potentiate epidermal cell adhesion and barrier formation
Kaelyn D. Sumigray, Henry P. Foote, and Terry Lechler

527 N-WASP coordinates the delivery and F-actin–mediated capture of MT1-MMP at invasive pseudopods
Xinzi Yu, Tobias Zech, Laura McDonald, Esther Garcia Gonzalez, Ang Li, Iain Macpherson, Juliane P. Schwarz, Heather Spence, Kinga Futó, Paul Timpson, Colin Nixon, Yafeng Ma, Ines M. Anton, Balázs Visegrády, Robert H. Insall, Karin Oien, Karen Blyth, Jim C. Norman, and Laura M. Machesky

545 Substrate stiffness regulates cadherin-dependent collective migration through myosin-II contractility
Mei Rosa Ng, Achim Besser, Gaudenz Danuser, and Joan S. Brugge



At a wound edge, actomyosin contractility—indicated by activated myosin light chain (green)—is higher in epithelial cells plated on a rigid substrate (right) than in cells plated on a softer surface (left). Intercellular adhesions propagate this contractility to cells farther back in the epithelial sheet, allowing the cells to coordinate their collective migration so that they move faster and more persistently on stiffer substrates. The cells are also stained for actin (red) and DNA (blue).
Image © 2012 Ng et al.
See page 545.

JCB
THE JOURNAL OF CELL BIOLOGY
VOL. 199, NO. 4, NOVEMBER 12, 2012

NEWS

In This Issue

566
- ARL-13 SUMO wrestles receptors into cilia
- Dnm1's recruitment strategy
- The fellowship of the Z ring
  B. Short

In Focus

567
- Cdc42 helps cancer cells make their exit
  B. Short

People & Ideas

568
- Gaudenz Danuser: The symphony of the cell
  C. Sedwick

Features

571 Cell biology: A key driver of therapeutic innovation
Oliver Hantschel and Giulio Superti-Furga

577 New frontiers in human cell biology and medicine: Can pluripotent stem cells deliver?
Lawrence S.B. Goldstein

583 Development of proteasome inhibitors as research tools and cancer drugs
Alfred L. Goldberg

RESEARCH ARTICLES

Reports

589 SUMOylation of the small GTPase ARL-13 promotes ciliary targeting of sensory receptors
Yujie Li, Qing Zhang, Qing Wei, Yuxia Zhang, Kun Ling, and Jinghua Hu

Articles

599 Characterization of the insertase for β-barrel proteins of the outer mitocnondrial membrane
Astrid Klein, Lars Israel, Sebastian W.K. Lackey, Frank E. Nargang, Axel Imhof, Wolfgang Baumeister, Walter Neupert, and Dennis R. Thomas

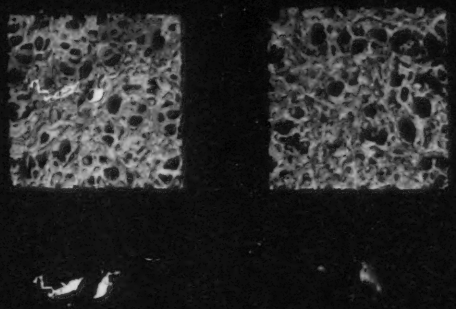
613 A novel motif in the yeast mitochondrial dynamin Dnm1 is essential for adaptor binding and membrane recruitment
Huyen T. Bui, Mary A. Karren, Debjani Bhar, and Janet M. Shaw

623 Distinct functions of chloroplast FtsZ1 and FtsZ2 in Z-ring structure and remodeling
Allan D. TerBush and Katherine W. Osteryoung

639 A flagellar A-kinase anchoring protein with two amphipathic helices forms a structural scaffold in the radial spoke complex
Priyanka Sivadas, Jennifer M. Dienes, Martin St. Maurice, William D. Meek, and Pinfen Yang

653 Cdc42 promotes transendothelial migration of cancer cells through β1 integrin
Nicolas Reymond, Jae Hong Im, Ritu Garg, Francisco M. Vega, Barbara Borda d'Agua, Philippe Riou, Susan Cox, Ferran Valderrama, Ruth J. Muschel, and Anne J. Ridley

Articles with related stories in the IN THIS ISSUE section have page numbers in RED; articles related to the IN FOCUS feature have page numbers in BLUE.



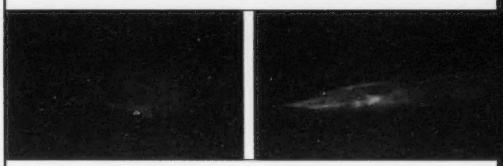
On the cover

Prostate cancer cells (yellow, left) extend multiple protrusions toward the endothelial cells (red) lining blood vessels in the mouse lung, whereas prostate cancer cells lacking Cdc42 (blue, right) remain rounded and show reduced spreading on the vessel walls. Reymond et al. reveal that Cdc42 promotes metastasis by inducing the expression of β1-integrin, boosting cancer cells' attachments to endothelial cells and the underlying basement membrane.
Image © 2012 Reymond et al.
See page 653.

669 **Crawling from soft to stiff matrix polarizes the cytoskeleton and phosphoregulates myosin-II heavy chain**
Matthew Raab, Joe Swift, P.C. Dave P. Dingal, Palak Shah, Jae-Won Shin, and Dennis E. Discher

685 ***Drosophila* PATJ supports adherens junction stability by modulating Myosin light chain activity**
Arnab Sen, Zsanett Nagy-Zsvér-Vadas, and Michael P. Krahn

699 **The C-terminal unique region of desmoglein 2 inhibits its internalization via tail–tail interactions**
Jing Chen, Oxana E. Nekrasova, Dipal M. Patel, Jodi L. Klessner, Lisa M. Godsel, Jennifer L. Koetsier, Evangeline V. Amargo, Bhushan V. Desai, and Kathleen J. Green



Cells tend to migrate from softer to stiffer matrices, a phenomenon known as durotaxis. Raab et al. demonstrate that this process relies on myosin-IIB (green), which is distributed uniformly in cells migrating on soft matrices (left) but polarizes toward the rear of the cell on stiffer ones (right). The cells are also stained for F-actin (red).
Image © 2012 Raab et al.
See page 669.

JCB
THE JOURNAL OF CELL BIOLOGY
VOL. 199, NO. 5, NOVEMBER 26, 2012

NEWS

In This Issue

714 • Why a microRNA's absence makes the heart grow larger
• A SIMPLE explanation for Charcot-Marie-Tooth disease
• Global sourcing for ring construction
B. Short

In Focus

715 • KIF4 helps mitotic chromosomes get in shape
B. Short

People & Ideas

716 • Stefano Bertuzzi: Science first
C. Sedwick

REVIEWS

Comments

719 Flies stretch their cells to avoid a chromatin trap
Mar Carmena

Reviews

723 Lysosomal storage disorders: The cellular impact of lysosomal dysfunction
Frances M. Platt, Barry Boland, and Aarnoud C. van der Spoel

RESEARCH ARTICLES

Reports

735 Csi1 links centromeres to the nuclear envelope for centromere clustering
Haitong Hou, Zhou Zhou, Yu Wang, Jiang Wang, Scott B. Kalmer, Tatiana Kurchuk, Elizabeth A. Miller, Fred Chang, and Sue Biggins

745 Cell elongation is an adaptive response for clearing long chromatid arms from the cleavage plane
Shaila Kotadia, Emilie Montembault, William Sullivan, and Anne Royou

Articles

755 Mitotic chromosomes are compacted laterally by KIF4 and condensin and axially by topoisomerase IIα
Kumiko Samejima, Itaru Samejima, Paola Vagnarelli, Hiromi Ogawa, Giulia Vargiu, David A. Kelly, Flavia de Lima Alves, Alastair Kerr, Laura C. Green, Damien F. Hudson, Shinya Ohta, Carol A. Cooke, Christine J. Farr, Juri Rappsilber, and William C. Earnshaw

771 Rlp24 activates the AAA-ATPase Drg1 to initiate cytoplasmic pre-60S maturation
Lisa Kappel, Mathias Loibl, Gertrude Zisser, Isabella Klein, Gernot Fruhmann, Christof Gruber, Stefan Unterweger, Gerald Rechberger, Brigitte Pertschy, and Helmut Bergler

783 Mutual antagonism between IP_3RII and miRNA-133a regulates calcium signals and cardiac hypertrophy
Faye M. Drawnel, Dagmar Wachten, Jeffery D. Molkentin, Marjorie Maillet, Jan Magnus Aronsen, Fredrik Swift, Ivar Sjaastad, Ning Liu, Daniele Catalucci, Katsuhiko Mikoshiba, Chihiro Hisatsune, Hanneke Okkenhaug, Simon R. Andrews, Martin D. Bootman, and H. Llewelyn Roderick

Articles with related stories in the IN THIS ISSUE section have page numbers in RED; articles related to the IN FOCUS feature have page numbers in BLUE; articles with COMMENTS have page numbers in GREEN.

On the cover

A surface-rendered 3D image shows the distribution of the ryanodine receptor II (green) and inositol-(1,4,5) triphosphate receptor II (IP_3RII, red) calcium channels in a cropped region of a rat ventricular cardiomyocyte. Drawnel et al. describe a positive feedback loop involving IP_3RII and the microRNA miR-133a that promotes cardiomyocyte hypertrophy. Image © 2012 Drawnel et al.
See page 783.

799 Charcot-Marie-Tooth disease-linked protein SIMPLE functions with the ESCRT machinery in endosomal trafficking
Samuel M. Lee, Lih-Shen Chin, and Lian Li

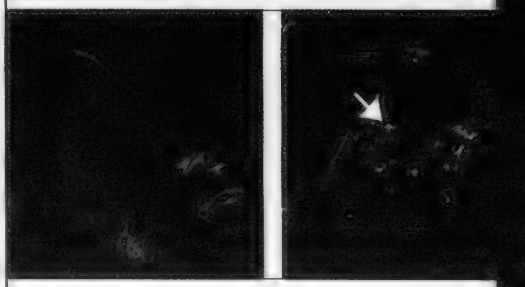
817 MARCH2 promotes endocytosis and lysosomal sorting of carvedilol-bound β_2-adrenergic receptors
Sang-oh Han, Kunhong Xiao, Jihee Kim, Jiao-Hui Wu, James W. Wisler, Nobuhiro Nakamura, Neil J. Freedman, and Sudha K. Shenoy

831 Nonmedially assembled F-actin cables incorporate into the actomyosin ring in fission yeast
Junqi Huang, Yinyi Huang, Haochen Yu, Dhivya Subramanian, Anup Padmanabhan, Rahul Thadani, Yaqiong Tao, Xie Tang, Roland Wedlich-Soldner, and Mohan K. Balasubramanian

849 Reconstitution of dynamic microtubules with *Drosophila* XMAP215, EB1, and Sentin
Wenjing Li, Takashi Moriwaki, Tomomi Tani, Takashi Watanabe, Kozo Kaibuchi, and Gohta Goshima

Corrections

863 The Sec1p/Munc18 (SM) protein, Vps45p, cycles on and off membranes during vesicle transport
Nia J. Bryant and David E. James



The β_2-adrenergic receptor (green) is expressed at the surface of control vascular smooth muscle cells (left) but is trafficked to lysosomes (red) upon treatment with the β blocker carvedilol (right). Han et al. reveal that carvedilol induces the receptor's endocytosis and lysosomal trafficking by promoting its association with the E3 ubiquitin ligase MARCH2.
Image © 2012 Han et al.
See page 817.

JCB
THE JOURNAL OF CELL BIOLOGY

NEWS

In This Issue

866
- Release notes for dense-core vesicles
- Opening up the ER's gatekeeper
- Segregating Bub1's mitotic functions

B. Short

In Focus

867
- Farp1 gives both sides of the story

B. Short

People & Ideas

868
- John Heuser: Capture the moment

C. Sedwick

REVIEWS

Reviews

871 Linking abnormal mitosis to the acquisition of DNA damage
Neil J. Ganem and David Pellman

RESEARCH ARTICLES

Reports

883 Munc13 controls the location and efficiency of dense-core vesicle release in neurons
Prescott de Bospoort, Margherita Farina, Sacha K. Schmitz, Arthur de Jong, Heidi de Wit, Matthijs Verhage, and Ruud F. Toonen

Articles

893 Variant repeats are interspersed throughout the telomeres and recruit nuclear receptors in ALT cells
Dimitri Conomos, Michael D. Stutz, Mark Hills, Ave A. Neumann, Tracy M. Bryan, Peggy P. Reddel, and Hilda A. Pickett

907 A gating motif in the translocation channel sets the hydrophobicity threshold for signal sequence function
Steven F. Trueman, Elisabet C. Mandon, and Reid Gilmore

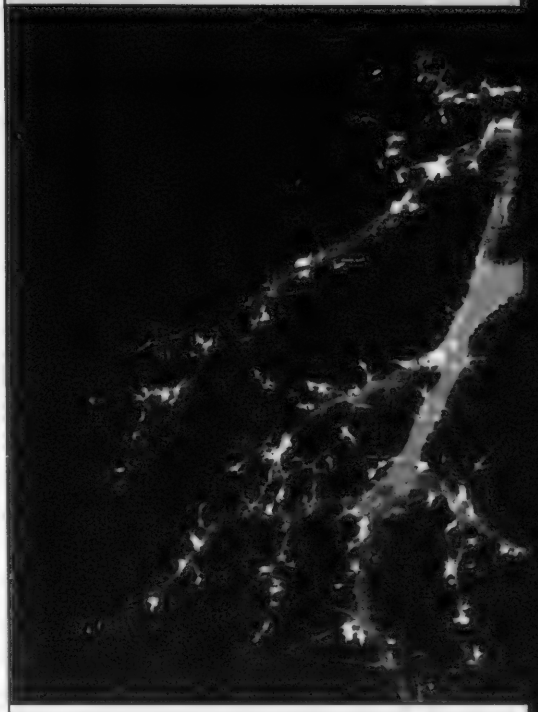
919 Mobility of the SecA 2-helix-finger is not essential for polypeptide translocation via the SecYEG complex
Sarah Whitehouse, Vicki A.M. Gold, Alice Robson, William J. Allen, Richard B. Sessions, and Ian Collinson

931 Bub1 kinase activity drives error correction and mitotic checkpoint control but not tumor suppression
Robin M. Ricke, Karthik B. Jeganathan, Liviu Malureanu, Andrew M. Harrison, and Jan M. van Deursen

951 KIF14 negatively regulates Rap1a–Radil signaling during breast cancer progression
Syed M. Ahmed, Brigitte L. Thériault, Maruti Uppalapati, Catherine W.N. Chiu, Brenda L. Gallie, Sachdev S. Sidhu, and Stéphane Angers

969 Local phosphocycling mediated by LOK/SLK restricts ezrin function to the apical aspect of epithelial cells
Raghuvir Viswanatha, Patrice Y. Ohouo, Marcus B. Smolka, and Anthony Bretscher

Articles with related stories in the IN THIS ISSUE section have page numbers in RED; articles related to the IN FOCUS feature have page numbers in BLUE.



On the cover

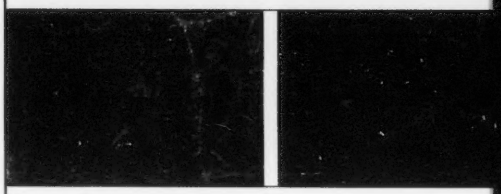
GFP-Farp1 (green) promotes the polymerization of F-actin (red) in dendritic spines, the postsynaptic protrusions of excitatory synapses. Cheadle and Biederer reveal that Farp1 works with the synaptic adhesion molecule SynCAM 1 to promote spine assembly and organize presynaptic active zones. The postsynaptic marker Shank is stained blue.

Image © 2012 Cheadle and Biederer.

See page 985.

985 The novel synaptogenic protein Farp1 links postsynaptic cytoskeletal dynamics and transsynaptic organization
Lucas Cheadle and Thomas Biederer

1003 PtdIns4P synthesis by PI4KIIIα at the plasma membrane and its impact on plasma membrane identity
Fubito Nakatsu, Jeremy M. Baskin, Jeeyun Chung, Lukas B. Tanner, Guanghou Shui, Sang Yoon Lee, Michelle Pirruccello, Mingming Hao, Nicholas T. Ingolia, Markus R. Wenk, and Pietro De Camilli



Compared with control cells (left), epithelial cells treated with the kinase inhibitor staurosporine (right) lack apical microvilli containing actin (red) and ezrin (green). Viswanatha et al. describe how ezrin's apical localization and function in microvillar assembly is regulated by a phosphorylation cycle involving the kinases LOK and SLK.
Image © 2012 Viswanatha et al.
See page 969.

JCB
THE JOURNAL OF CELL BIOLOGY
VOL. 199, NO. 7, DECEMBER 24, 2012

NEWS

In This Issue

1018 • Apoptotic regulators dispose of the midbody
• Secretory proteins hail a cab at the TGN
• How endothelial junctions get deep-Syx'd
B. Short

In Focus

1019 • Lkb1 takes different paths to morphogenesis
B. Short

People & Ideas

1020 • Li-Huei Tsai: I well remember
C. Sedwick

REVIEWS

Comments

1023 Cell height: Tao rising
Liang Cai and Keith E. Mostov

Reviews

1025 Mitotic spindle (DIS)orientation and DISease: Cause or consequence?
Anna Noatynska, Monica Gotta, and Patrick Meraldi

RESEARCH ARTICLES

Reports

1037 Nucleotide excision repair–initiating proteins bind to oxidative DNA lesions in vivo
Hervé Menoni, Jan H.J. Hoeijmakers, and Wim Vermeulen

1047 Apoptotic regulators promote cytokinetic midbody degradation in *C. elegans*
Yongping Chai, Dong Tian, Yihong Yang, Guoxin Feng, Ze Cheng, Wei Li, and Guangshuo Ou

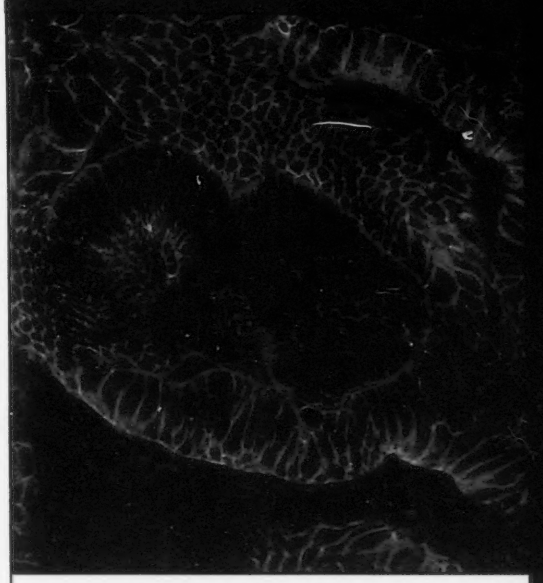
1057 Cab45 is required for Ca^{2+}-dependent secretory cargo sorting at the trans-Golgi network
Julia von Blume, Anne-Marie Alleaume, Christine Kienzle, Amado Carreras-Sureda, Miguel Valverde, and Vivek Malhotra

Articles

1067 The chromatin remodeler p400 ATPase facilitates Rad51-mediated repair of DNA double-strand breaks
Céline Courilleau, Catherine Chailleux, Alain Jauneau, Fanny Grimal, Sébastien Briois, Elisa Boutet-Robinet, François Boudsocq, Didier Trouche, and Yvan Canitrot

1083 Cep164 mediates vesicular docking to the mother centriole during early steps of ciliogenesis
Kerstin N. Schmidt, Stefanie Kuhns, Annett Neuner, Birgit Hub, Hanswalter Zentgraf, and Gislene Pereira

Articles with related stories in the IN THIS ISSUE section have page numbers in RED; articles related to the IN FOCUS feature have page numbers in BLUE; articles with COMMENTS have page numbers in GREEN.



On the cover

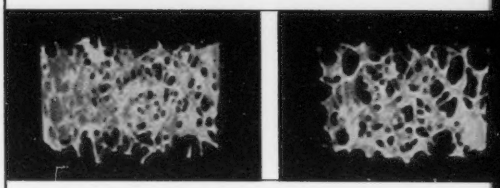
When the tumor suppressor Lkb1 is inhibited in explants of embryonic pancreas, epithelial structures that resemble precancerous lesions are formed even though cell polarity—indicated by actin (red) and the basolateral marker EpCAM (green)—remains intact. Lo et al. use chemical genetics and ex vivo cultures to identify distinct Lkb1-dependent pathways in tissue morphogenesis and cancer development.
Image © 2012 Lo et al.
See page 1117.

1103 VEGF and Angiopoietin-1 exert opposing effects on cell junctions by regulating the Rho GEF Syx
Siu P. Ngok, Rory Geyer, Miaoliang Liu, Antonis Kourtidis, Sudesh Agrawal, Chuanshen Wu, Himabindu Reddy Seerapu, Laura J. Lewis-Tuffin, Karen L. Moodie, Deborah Huveldt, Ruth Marx, Jay M. Baraban, Peter Storz, Arie Horowitz, and Panos Z. Anastasiadis

1117 Lkb1 regulates organogenesis and early oncogenesis along AMPK-dependent and -independent pathways
Bryan Lo, Geraldine Strasser, Meredith Sagolla, Cary D. Austin, Melissa Junttila, and Ira Mellman

1131 Tao controls epithelial morphogenesis by promoting Fasciclin 2 endocytosis
Juan Manuel Gomez, Ying Wang, and Veit Riechmann

1145 Plasma membrane calcium ATPase regulates bone mass by fine-tuning osteoclast differentiation and survival
Hyung Joon Kim, Vikram Prasad, Seok-Won Hyung, Zang Hee Lee, Sang-Won Lee, Aditi Bhargava, David Pearce, Youngkyun Lee, and Hong-Hee Kim



Kim et al. reveal that the plasma membrane calcium ATPases PMCA1 and PMCA4 regulate the differentiation and survival of bone-resorbing osteoclasts. Micro-computed tomography of femurs from wild-type (left) and PMCA4-null mice (right) demonstrate that bone mass is reduced in the absence of PMCA4. Image © 2012 Kim et al.
See page 1145.